GROWTH FACTOR PROPERTIES OF VIP DURING EARLY BRAIN DEVELOPMENT: WHOLE EMBRYO CULTURE AND IN VIVO STUDIES. Pierre Gressens[1], Joanna M. Hill[2], Illana Gozes[3], Philippe Evrard[1] and Douglas E. Brenneman[2]. 1. Lab. Neurol. Devel., Hopital Robert-Debre, Paris, France; 2. Lab. of Devel. Neurobiol, NICHD, NIH, Bethesda, MD, USA; 3. Dept. of Clin. Biochem., Tel Aviv Univ., Tel Aviv, Israel.

To address the potential effects of VIP on embryonic growth, whole post-implantation embryo cultures were utilized. After a 4-hour incubation, VIP stimulated growth as assessed by the following increases from control: embryonic volume (63%), DNA (103%) and protein content (63%), and number of cells in S-phase (490%). The effects of VIP on the different phases of the cell cycle of neural cells were studied with cumulative labeling of S phase cells by incorporation of BRDU: S phase and G1 phase of neuroepithelial cells were shortened by 46% and 57% respectively. Consequently, the length of the mitotic cycle was reduced by 40%.

To assess the *in vivo* function of VIP in early CNS growth, a VIP antagonist (VA) was IP injected between E9 and E11. VA induced a dose-dependent reduction of the DNA (84% of controls) and protein (80% of controls) in brain. In contrast, body growth was less affected by the antagonist. Injections of VA for a longer period (E9 to E17) did not increase the severity of the microcephaly.

By *in vitro* autoradiography, VIP binding sites were detected in the germinative neuroepithelium between E9 and E11 but not beyond E12, during neuronal migration.

These data demonstrate that VIP regulates mitogenic activity by shortening S and G1 phases in the premigratory neuroepithelium. Although this effect is limited to a short ontogenic period, blockage of VIP by a specific antagonist induces a severe microcephaly.